

CONTACT: Clare Collins  
412-641-7299  
412-770-8643 (mobile)  
collex@upmc.edu

## QUESTIONS AND ANSWERS

### MTN-035 (DESIRE)

#### Acceptability, Tolerability and Adherence to Three Rectal Microbicide Placebo Methods

##### What is the aim of the DESIRE study?

[MTN-035](#), or DESIRE (Developing and Evaluating Short-acting Innovations for Rectal Use), is an open label crossover study to systematically examine three methods for delivering drugs to help prevent HIV infection from anal sex. The approach used in DESIRE will assess participants' preferences for a rectal delivery method before specific products have been developed, and, importantly, after they have had an opportunity to use it.

##### Who is conducting and funding the study?

MTN-035 is a study of the [Microbicide Trials Network](#) (MTN), an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health (NIH). The protocol chair for the study is José A. Bauermeister, Ph.D., M.P.H., of the University of Pennsylvania School of Nursing.

##### Why is this study important?

Anal sex is a common sexual behavior practiced by cisgender and transgender men and women around the world. According to some estimates, the risk of becoming infected with HIV during anal sex is 20 times greater than during vaginal sex because the rectal lining is thinner and more fragile than the vaginal lining. While condoms are an effective method to prevent HIV infection through anal sex, many people can't or don't want to use them every time they have sex. Similarly, oral pre-exposure prophylaxis (PrEP) – an HIV prevention strategy in which people take a daily pill called Truvada® to prevent infection – has been shown to be highly effective, however, not all people vulnerable to HIV infection are willing or able to access it.

Rectal microbicides – products in the form of gels, douches, fast-dissolving rectal inserts and suppositories that are being developed and tested to reduce a person's risk of HIV or other sexually transmitted infections through anal sex – could give people an additional choice for HIV prevention, one that is non-systemic and used around the time of sex. By testing a variety of placebo delivery methods for HIV prevention, MTN-035 will impact the development of intervention strategies for future drug trials of rectal microbicides.

##### When will the study begin and how long will it last?

The study began in February 2019, with results anticipated in 2020.

##### Where will DESIRE be conducted?

MTN-035 is being conducted at the following trial sites (pending necessary approvals): the Blantyre Clinical Research Site (CRS) in Malawi; the IMPACTA CRS in Lima, Peru; the Wits Reproductive Health and HIV Institute in Johannesburg, South Africa; the Chiang Mai University HIV Prevention CRS in Thailand; and, the University of Pittsburgh CRS, the Bridge HIV CRS in San Francisco, and the University of Alabama at Birmingham CRS in the United States.

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### **What methods are being studied in MTN-035?**

The rectal delivery methods being tested in MTN-035 include a [placebo douche](#), a [placebo suppository](#) and a [placebo insert](#) (a fast-dissolving rectal tablet). The insert was developed by CONRAD, a not-for-profit research and development organization located in Arlington, Va.

### **Why study placebo products?**

By evaluating several placebo approaches for delivering rectal microbicides, MTN-035 will give researchers a better sense about individual preferences, which is important for predicting actual product use. Learning about participants' experiences with placebo methods will also help researchers address any barriers participants may experience in using specific products in the future.

### **What is known about douching and receptive anal sex?**

Cisgender and transgender people who practice receptive anal sex often report douching before or after sex. In a published review of douching practice among cisgender men who have sex with men, 88 percent reported having douched before receptive anal sex. Given the popularity of douching in preparation for anal sex, a microbicide delivered in this manner could have high acceptability and uptake among people who engage in receptive anal sex.

### **How is DESIRE designed?**

MTN-035 is designed to evaluate the acceptability, tolerability and adherence to three methods for delivering drugs to help prevent HIV infection from receptive anal sex. Study participants will use each rectal delivery method for a month at a time, with a week-long break between methods. They will be asked to use each method between 30 minutes and 3 hours prior to engaging in receptive anal sex, or once a week for participants who have not engaged in receptive anal sex in a given week.

During MTN-035, study participants will be asked about their preferences and the likelihood that they would use the approaches if effective and available. Researchers will also assess the safety of each method and evaluate whether participants used them correctly and consistently. As part of the study, all participants will receive HIV risk reduction counseling and condoms and will be tested for HIV and sexually transmitted infections.

### **How many people will be enrolled into DESIRE?**

The study will include approximately 210 HIV-negative cisgender men, transgender men and transgender women who have sex with men at sites in Malawi, Peru, South Africa, Thailand and the United States.

### **Why aren't cisgender women being enrolled into DESIRE?**

Although cisgender women report engaging in receptive anal sex and have been included in early rectal microbicide studies, MTN-035 is focusing on populations *most* vulnerable to HIV infection from receptive anal sex. This includes cisgender men who have sex with men and transgender individuals.

### **What is being done to ensure the safety of the participants?**

MTN-035 was designed according to stringent ethical and scientific guidelines with numerous measures to protect the safety and well-being of participants. As with all NIH-funded studies, the study incorporates a multi-tiered safety review process and is conducted with oversight by regulatory and research authorities. The protocol has undergone rigorous review by NIAID, institutional review boards and in-country regulatory and ethics bodies.

### **Will participants in the study provide informed consent?**

Written informed consent will be obtained from potential participants prior to screening and enrollment in MTN-035. This will ensure that individuals understand the study procedures, and possible risks and benefits. Individuals will be under no obligation to participate in the study and can leave it at any time, without consequence.

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### **Why are rectal microbicides needed?**

Worldwide, nearly 37 million people are currently living with HIV. Since the epidemic began in the early 1980s, about 77 million people have been infected with the virus and 39 million people have died of HIV-related causes. Although the rate of new infections has stabilized in many countries around the world, HIV continues to disproportionately affect young cisgender women and girls, people of color, gay men and other men who have sex with men, and transgender women. If shown to be safe and effective, a rectal microbicide could give people who practice anal sex an additional option to protect themselves against HIV infection.

### **What other products are being tested as rectal microbicides?**

DESIRE is part of a research agenda at the MTN focused on the development of non-systemic HIV prevention products for men and women who engage in condomless anal sex, a major risk factor for HIV infection. Unlike systemic drugs, such as pills, which work throughout the body, microbicides are intended to work at the site of potential infection.

MTN researchers reported results from the first Phase II study of a rectal microbicide, a gel containing the antiretroviral (ARV) drug tenofovir, in early 2016. The study, [MTN-017](#), evaluated whether a reduced-glycerin formulation of tenofovir gel was safe and acceptable as a rectal microbicide. Results indicated that the gel used in MTN-017 was safe, with most study participants highly adherent to it. The gel was found most acceptable when used around the time of sex, rather than daily. Some participants, however, expressed dissatisfaction with the gel delivery method, a plastic applicator, prompting researchers to continue to explore other formulations and delivery methods for rectal microbicides.

Two other MTN rectal microbicide studies have recently been completed, [MTN-026](#) and [MTN-033](#), and another study, [MTN-037](#), has been fully enrolled. MTN-026 and MTN-033 evaluated the rectal safety and pharmacokinetics of a gel based on dapivirine, an ARV that prevents HIV from replicating, while MTN-037 is evaluating the safety of a multipurpose gel, PC-1005, developed by the Population Council to prevent HIV, herpes simplex virus (HSV) and human papillomavirus (HPV) simultaneously. HPV infection is common among men who have sex with men and is a primary risk factor for developing anal cancer, while HSV increases susceptibility to HIV. PC-1005 is the only product designed for vaginal and rectal use targeting all three sexually transmitted infections that has undergone a Phase 1 study to date.

Other research-based programs include DREAM (Delivery of Rectal Enema as Microbicide), which is exploring the delivery of tenofovir as a single-dose enema and PREVENT (Griffithsin-based Rectal Microbicides for PREvention of Viral ENTry), which is addressing the need for a non-ARV based rectal microbicide. Both DREAM and PREVENT are funded by NIH.

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### **About the Microbicide Trials Network**

*The Microbicide Trials Network (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners whose work is focused on the rigorous evaluation of promising microbicides – products applied inside the vagina or rectum that are intended to prevent the sexual transmission of HIV – from the earliest phases of clinical study to large-scale trials that support potential licensure of these products for widespread use. More information about the MTN is available at <https://mtnstopshiv.org>.*